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## Sagittal Abdominal Diameter and Visceral Adiposity:

### Correlates of Beta-Cell Function and Dysglycemia in Severely Obese Women

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## Abstract

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**Background**—In the context of increasing obesity prevalence, the relationship between large visceral adipose tissue (VAT) volumes and type 2 diabetes mellitus (T2DM) is unclear. In a clinical sample of severely obese women (mean body mass index [BMI], 46 kg/m<sup>2</sup>) with fasting normoglycemia ( $n=40$ ) or dysglycemia (impaired fasting glucose+diabetes;  $n=20$ ), we sought to determine the usefulness of anthropometric correlates of VAT and associations with dysglycemia.

**Methods**—VAT volume was estimated using multi-slice computer tomography; anthropometric surrogates included sagittal abdominal diameter (SAD), waist circumference (WC) and BMI. Insulin sensitivity (Si), and beta-cell dysfunction, measured by insulin secretion (AIRg) and the disposition index (DI), were determined by frequently sampled intravenous glucose tolerance test.

**Results**—Compared to fasting normoglycemic women, individuals with dysglycemia had greater VAT ( $P<0.001$ ) and SAD ( $P=0.04$ ), but BMI, total adiposity and Si were similar. VAT was inversely associated with AIRg and DI after controlling for ancestry, Si, and total adiposity (standardized beta,  $-0.32$  and  $-0.34$ , both  $P<0.05$ ). In addition, SAD (beta= $0.41$ ,  $P=0.02$ ) was found to be a better estimate of VAT volume than WC (beta= $0.32$ ,  $P=0.08$ ) after controlling for covariates. Receiver operating characteristic analysis showed that VAT volume, followed by SAD, outperformed WC and BMI in identifying dysglycemic participants.

**Conclusions**—Increasing VAT is associated with beta-cell dysfunction and dysglycemia in very obese women. In the presence of severe obesity, SAD is a simple surrogate of VAT, and an indicator of glucose dysregulation.

## Keywords

Obesity; Type 2 diabetes; Waist circumference; Anthropometry; Intra-abdominal fat; Insulin resistance; Sagittal abdominal diameter

## Introduction

In the United States during the years 1988 to 2008, the increasing prevalence in obesity occurred mainly in the categories of severe obesity (body mass index [BMI]  $\geq 40$  kg/m<sup>2</sup>), which doubled (from 2.9 % to 5.7 %), and moderate obesity (BMI, 35–40 kg/m<sup>2</sup>), which tripled (from 5.2 % to 14.3 %), compared to mild obesity (BMI, 30–35 kg/m<sup>2</sup>), which increased by 37 % [1]. Although in part these increases are a function of a smaller baseline, these trends are alarming since individuals with more extreme obesity carry the largest burden of cardiometabolic disease. For example, the risk of developing type 2 diabetes mellitus (T2DM) is 7-fold higher in those with a BMI  $\geq 40$  kg/m<sup>2</sup> compared to those with a BMI  $\geq 25$  kg/m<sup>2</sup> [2]. However, only one-third of those with severe obesity exhibit diagnosed and undiagnosed T2DM [3], demonstrating that in addition to obesity, other factors are at play in producing glucose dysregulation.

It is well recognized that abdominal adiposity is a greater determinant of diabetes risk than general adiposity [4, 5]. Evidence also shows that diabetes risk, as well as its underlying pathologies, insulin resistance and beta-cell dysfunction, are associated with visceral adiposity in cross-sectional [6, 7] and longitudinal studies [8–10]. However, the aforesaid populations studied were overweight or mildly obese and may not be representative of individuals who carry large amounts of adipose tissue. In individuals with high adiposity it has been previously observed that the relationship between insulin resistance and general or visceral adipose tissue (VAT) may be complicated, such that development of further obesity in an individual may not result in proportional increases in insulin resistance [11]. Cnop et al. [12] also report a nonlinear relationship between intra-abdominal fat and insulin sensitivity, especially at high levels of central adiposity. Thus in severely obese women — who we have previously shown carry a wide range of visceral fat (1–8 l) [13] — the impact

of this depot on the dynamics of insulin sensitivity and beta-cell function is not well understood. This is of greater interest given the recent information that ectopic fat storage in the pancreas increases with increasing visceral adiposity [14, 15].

The volume of VAT is best estimated by computed tomography or magnetic resonance imaging (MRI), but these techniques are not feasible in the clinical or population setting. Visceral adiposity can also be estimated by the waist circumference (WC) or the sagittal abdominal diameter (SAD), which measures the vertical anterior-to-posterior distance when the subject is supine. These external measures have been validated [16, 17] and are more practical than tomography or MRI since they are low-cost and non-invasive. WC is the more widely used measure and is accepted by the American Heart Association/National Heart, Lung, and Blood Institute and other leading organizations as a diagnostic criterion for metabolic syndrome [18]. However, particularly for obese women, limited data suggest that WC is a poorer predictor of VAT than other anthropometric measures, including SAD [10, 19, 20]. Moreover, WC may be difficult to obtain in individuals with large abdomens and the usefulness of WC in estimating disease risk in the severely obese has been questioned [21].

BMI, an indicator of generalized adiposity, is commonly used in clinical practice. However, indicators of abdominal adiposity may be better markers of dysglycemia in women since the association between VAT and incident diabetes is stronger in women compared to men [9]. Therefore, the purpose of this paper was to assess anthropometric correlates, SAD, WC, and BMI, for the identification of VAT volume and dysglycemia (impaired fasting glucose or T2DM) in moderately and severely obese women. Additionally, we examined the relationship between VAT and insulin action in this patient population across the spectrum of glucose tolerance. Findings demonstrate the validation of SAD as a marker of visceral adiposity and dysglycemia in highly adipose women and the significant associations between visceral adiposity and beta-cell dysfunction in this population.

## Materials and Methods

### Patients

The study included 60 women with high adiposity who were weight stable (no more than  $\pm 2$  kg during the week before testing) while undergoing evaluation before initiation of weight management therapy at the Emory Bariatric Clinic. Ninety-five percent of the participants were seeking bariatric surgery. Exclusion criteria for this study were male sex (since the relationship between VAT and diabetes risk depends on sex) [9] and age less than 19 years or greater than 65. Based upon clinical history and fasting plasma glucose (FPG) concentrations, individuals were categorized as having fasting normoglycemia (never treated with hypoglycemic drugs and FPG  $< 5.6$  mmol/l,  $n=40$ ) or dysglycemia (physician-documented diabetes history [ $n=7$ ] or FPG  $\geq 5.6$  mmol/l,  $n = 13$ ) [22]. The Emory University Institutional Review Board approved the study (#333-2002); patients were recruited as a convenient sample during May 2003 and March 2009, and all patients signed informed consent prior to enrollment.

### Anthropometry and Body Fat Composition

Body weight, height, and all other body composition measurements were obtained with participants in light clothing, without shoes, in the fasting state, immediately after voiding in the morning and, except for the SAD, in the standing position. The WC was obtained by tape measure at the smallest point of the posterior torso between the inferior rib and the iliac crest. The SAD was obtained between the iliac crest and the lowest palpable rib, with subjects lying supine and at the end of a normal expiration, using an expanded Holtain–

Kahn caliper (Holtain Ltd, Crymych, UK). Body fat was measured by air displacement plethysmography (BOD-POD, Life Measurement Instruments, Concord, CA) [13]. Abdominal fat distribution was measured by computed tomography (CT), using a GE High Speed Advantage CT scanner (General Electric Medical Systems, Milwaukee, WI) as described [13]. Volumes of VAT and subcutaneous adipose tissue (SAT), respectively, were determined from CT scans taken from the L1 to the L5 vertebral region (140 kV, 240–340 mAs, 10-mm slice thickness). Adipose tissue within an attenuation range of –190 to –30 Hounsfield units was highlighted and computed using software (GE Medical Systems) [13].

### Glucose Tolerance Testing

The insulin-modified frequently sampled intravenous glucose tolerance test (FSIGTT) [13] was chosen to assess insulin action in vivo, as it provides information about peripheral insulin sensitivity and first-phase insulin secretion for the calculation of the disposition index (DI) in a single test. Patients were admitted into the Emory General Clinical Research Center on the night before the FSIGTT test and fasted overnight (12 h). Seven patients with T2DM were taking various antihyperglycemic medications including metformin, sulfonylureas, thiazolidinediones, glucagon-like peptide 1 agonists, and insulin, which were adjusted so that baseline glucose levels were close to normal but withheld from patients on the morning of intravenous glucose tolerance testing. Plasma glucose was quantified at the Emory University Hospital Laboratory using the Beckman Coulter Alex 20 automated system; assay limit 0.17 mM (Beckman Coulter, Brea, CA). Hemoglobin A1c was measured by high performance liquid chromatography. Insulin was measured by immunoassay; assay limits 1  $\mu$ U/ml (for Regular assay) and 0.07  $\mu$ U/ml (for Ultrasensitive assay), respectively with less than 1 % cross-reactivity to proinsulin and c-peptide (Mercordia, Winston-Salem, NC). Minimal modeling analysis using the software program MinMod Millennium version 6.02 (MinMod Millennium, Los Angeles, CA) [23] was used to quantify insulin sensitivity (Si), first phase insulin secretion (AIRg) and the DI ( $DI = AIRg \times Si$ ). The disposition index is a quantification of beta-cell function by using a constant which describes an individual's insulin secretion response for a prevailing level of insulin sensitivity [11].

### Statistical Analysis

Before conducting the analyses, the data were screened for normality and parametric tests were used throughout. Continuous variables were presented as means  $\pm$  SD, and independent *t*-tests were used to compare the differences between normo- and dysglycemic women in the distribution of continuous variables. Categorical variables were presented as proportions, and these were compared between normo- and dysglycemic women using chi-square tests. Relationships between VAT volumes and anthropometric measures, as well as indices of insulin action, were examined using Pearson linear correlations and multiple regression analysis. Relationships among measures were also examined as general linear modeling analysis, including covariates for ancestry, menopausal status, age, total body fat mass and Si. Regression models were explored for multi-collinearity. For our models, variance inflation indices and tolerance statistics were well below 10 and above 0.2, respectively, confirming that there was no collinearity within our data. Receiver operating characteristic (ROC) curves, plots of sensitivity versus 1 – specificity, were generated to explore the ability of VAT, SAD, WC and BMI to identify women with impaired fasting glucose or T2DM. Area under the curve (AUC) was calculated to explore which of the above mentioned parameters showed the highest accuracy in identifying these same dysglycemic women. A maximum value of the Youden index was calculated as sensitivity + specificity – 1 and used as the optimal cut-off point for each of the parameters. The statistical software STATISTICA (StatSoft Inc., Tulsa, OK) and Statistical Package for Social Sciences version 19 (SPSS Inc., Armonk, NY) were used for study analysis. The significance level for the study was set at  $P < 0.05$ .

## Results

### Patient Characteristics

Patient characteristics, including adipose-tissue volumes, anthropometry, and metabolic indices, are described in Table 1. The mean age of the study population was  $36.7 \pm 9.2$  years and 12 % were post-menopausal. The group defined as hyperglycemic had higher blood hemoglobin A1c concentrations than the normoglycemic group ( $P=0.025$ ). There were similar proportions of self-described non-Hispanic African Americans and Caucasians (45 % and 48 %, respectively) in both fasting normoglycemic or dys-glycemic populations and the remaining women were Hispanic. Their BMIs ranged from 33.7 to 59.8 kg/m<sup>2</sup>; total adipose tissue from 44.8 to 119.6 kg; and abdominal subcutaneous adipose tissue from 7,360 to 27,600 cm<sup>3</sup>; the distribution of these values did not differ between participants who were normoglycemic or dysglycemic.

Despite similar adiposity in terms of BMI, total adipose tissue, and abdominal subcutaneous adipose tissue, women with dysglycemia presented greater volumes of VAT ( $P<0.001$ ) and its anthropometric correlate, SAD ( $P=0.038$ ), but not WC ( $P=0.41$ ), compared to normoglycemic women.

Peripheral insulin sensitivity was also similar between dysglycemic and normoglycemic women, although this was below normal when compared to normal reference values [24] (Table 1). However, first phase insulin secretion, AIRg, and DI — the ability to compensate for reduced insulin sensitivity — were all diminished (both  $P<0.001$ ) in women with dysglycemia.

### Associations Between Visceral Adiposity and Insulin Action

Since dysglycemic women had greater central obesity measured by VAT and SAD, we assessed the relationships between abdominal adiposity and insulin action. VAT was negatively correlated with indicators of insulin secretion (AIRg,  $r=-0.36$ ,  $P=0.006$ ; DI,  $r=-0.36$ ,  $P=0.005$ , respectively), but not with insulin sensitivity ( $r=0.06$ ,  $P=0.67$ ). In support of this finding, greater VAT was associated with higher FPG ( $r=0.33$ ,  $P=0.009$ ). General linear modeling was undertaken to assess the independent association of VAT with AIRg and DI (Table 2). The analysis revealed that AIRg was associated with VAT volume, after adjusting for Si, total adiposity, and ancestry (standardized beta coefficient= $-0.32$ ,  $P=0.022$ ). When age or menopausal status were included in the same model, the relationship between AIRg and VAT was no longer significant. Similarly, VAT volume predicted DI, regardless of Si, total adiposity and race (standardized beta coefficient= $-0.34$ ,  $P=0.013$ ). Moreover, the association between VAT volume and FPG remained independent of total adiposity and age (standardized beta coefficient= $0.38$ ,  $P=0.009$ ).

### Associations Between Visceral Adiposity and Anthropometric Indicators

Associations between computed tomography-determined VAT volume and either SAD or WC were evaluated to determine the better anthropometric measure of visceral adiposity. In multiple regression analysis, a greater effect size was associated with SAD (standardized beta= $0.42$ ,  $P<0.001$ ) versus WC (standardized beta= $0.27$ ,  $P=0.039$ ) for the outcome VAT (Table 3). After controlling for total adiposity, age, menopausal status, and ancestry, the effect of SAD on VAT remained significant (standardized beta= $0.39$ ,  $P=0.026$ ), whereas the association between VAT and WC was eliminated (standardized beta= $0.29$ ,  $P=0.123$ ).

### Identification of Dysglycemia by Abdominal Adiposity

Among the anthropometric measures BMI, SAD, and WC, we wished to determine the most suitable marker for detection of dysglycemia in this population of moderately obese to



severely obese women. In a multiple regression analysis containing BMI, SAD and WC together in the same model, only SAD was found to be associated with dysglycemia (standardized betas for SAD, BMI, and WC=0.42,  $P=0.041$ ,  $-0.10$ ,  $P=0.60$  and  $-0.11$ ,  $P=0.58$ , respectively). An independent evaluation using ROC curve analysis showed that the areas under the curve (AUCs) for VAT and SAD were significantly different from the reference line (for VAT, AUC=0.788, 95 % CI=0.663,0.912,  $P<0.001$ , for SAD, AUC=0.644, 95 % CI=0.516, 0.812,  $P<0.05$ ), whereas the AUCs for WC and BMI were comparable to the line (for WC, AUC=0.575, 95 % CI, 0.417, 0.733; for BMI, AUC=0.555, 95 % CI=0.400, 0.710) (Fig. 1). Of simple markers that could be utilized in clinical practice, SAD, compared to WC and BMI, performed better than chance in identifying correlates of VAT and dysglycemia in these obese women.

## Conclusion

The novel findings from this work in women with high adiposity are that the SAD was a better estimate of visceral adiposity and identifying dysglycemia compared to the more often used dimensions, WC and BMI. We also demonstrate that increasing visceral adiposity is independently and adversely associated with beta-cell function and dysglycemia.

The development of T2DM is related to poor insulin sensitivity combined with the inability to compensate through increased insulin secretion (i.e., beta-cell dysfunction) [11]. We and others have demonstrated that severely obese individuals commonly exhibit severe insulin resistance, but only those with inadequate beta-cell function are glucose intolerant [25, 26]. Some studies have shown that visceral, as compared to subcutaneous, adipose tissue disproportionately impairs insulin resistance and insulin secretion [6, 7]; however, most of the study populations were non- or mildly obese. In a few studies that have carefully explored these variables in individuals with greater degrees of adiposity, the relationships between insulin sensitivity and total or visceral fat depots were found to be non linear and to reach a threshold [12, 27]. The data from the population of moderately and severely obese women in the present study confirm these earlier findings and illustrate that individuals with extreme degrees of adiposity do not reflect the linear relationships usually noted between VAT depots and insulin sensitivity.

For beta-cell function, reports of relationships with VAT have been mixed, with some studies finding negative correlations [6, 7] or no effect [28]; the discrepancy may be due to differences in methodology for assessing beta-cell function (via intravenous versus oral glucose challenge). In the present study we found that visceral adiposity was negatively associated with first phase insulin secretion and beta-cell function, after controlling for race, total adiposity and Si. The inverse relationship between VAT and insulin secretion found in the present study is consistent with observations described in less-obese individuals of varying insulin resistance but without diabetes [6, 7]. To our knowledge, only one other study — in a smaller number of moderately obese and euglycemic individuals — measured first phase insulin secretion and VAT, and a modest, non-significant correlation was observed [29]. However relationships between visceral adiposity and beta-cell function may be more evident in the present study since participants had a wide range of glycemia. In the present study, we also demonstrate an independent and positive association between VAT and fasting glycemia which may be a manifestation of the inverse relationship between VAT and beta-cell function. Moreover, our finding also supports that of a longitudinal study which observed increases in visceral fat over time in pre-diabetic versus normoglycemic adolescents [30]. The biological mechanisms responsible for the association between VAT and beta-cell dysfunction are not yet clear. The lipotoxicity theory proposes that chronically elevated free fatty acids released from visceral fat, may promote oxidative stress and induce beta-cell apoptosis [31]. Ectopic deposition of fat into the pancreas, presumably from

expanded VAT stores has been recently demonstrated [14, 15], but the consequences, in vivo, of intra-pancreatic fat on beta-cell function have been inconsistent [14]. The findings from this current study do not address these proposed mechanisms.

We and others have shown that beta-cell function is a critical determinant for the maintenance of glucose homeostasis in the severely obese [25, 26]. Given the negative association observed between beta-cell function and VAT volume, we determined whether VAT serves as a marker of dysglycemia in women with high adiposity. ROC analysis showed that increased VAT volume identified individuals with impaired fasting glucose or T2DM with reasonable sensitivity and specificity. Since direct measurement of VAT is costly and can be invasive, we assessed the simple anthropometric measures SAD and WC for ability to estimate VAT volume. First, we found that SAD was a better estimate of VAT volume, compared with WC in moderately and severely obese women. In addition, SAD had a greater capacity to identify prevalence of dysglycemia compared to WC — which performed no better than BMI alone. Given the cross-sectional design of this current study, our findings only support the predictability of SAD for prevalence, but not risk of future diabetes (i.e., incidence). However our findings are supported by two recent longitudinal cohort studies which show that that SAD better predicted incident diabetes compared to BMI and WC alone [10, 32].

In severely obese women, the technique for measurement of WC — since it is obtained in the standing position — may be obtained with poorer reliability because of their larger girth, greater skin folds, sagging, and difficulties in locating landmarks [33]. Consistent with the finding in the present study, a validation study, using a small number of lean and obese men and women, found that SAD was better able to predict VAT compared to WC [34]. This finding has been replicated in other populations including Latin Americans and Asians [35, 36]. Among adults with high total fat mass, the correlation between VAT and WC was weaker than among persons with low total fat mass [37]. Studies in men have shown that SAD was more strongly associated with atherogenic lipoprotein particles [38], insulin resistance and hyperproinsulinemia [39] compared to WC. Beyond the correlations with physiologic disturbance, more specific anthropometric markers, other than BMI alone, may improve the screening for clinical diseases associated with high adiposity. For example, a substantial proportion of diabetes in the U.S. population is undiagnosed, and those affected are at greater risk for diabetes complications [40]. Epidemiological surveillance among very obese women could benefit from our finding that greater SAD, rather than WC or BMI, better identifies individuals at risk.

This study is particularly novel given the study of a population of women with high adiposity, the rigor of analysis of in vivo visceral adiposity and beta-cell function, the inclusion of African American participants, and the demonstration of the usefulness of SAD compared to BMI and WC in identifying increased VAT and its attendant risks for dysglycemia. A potential limitation of the FSIGTT approach is that insulin sensitivity may be underestimated in individuals with diabetes [41], but since beta-cell function may be of greater interest than is insulin sensitivity, the use of the FSIGTT in the current study is appropriate. The study was done only in women; it is possible that the relationships observed between VAT and SAD versus WC may not be generalizable to highly adipose men, who carry more VAT compared to women but exhibit a smaller range of variation in VAT at similar BMI [42]. Because this study is cross-sectional, it is not possible to determine if the link between visceral adiposity and beta-cell dysfunction is causal or also if visceral adiposity is the precursor. Finally, we do not have dietary or physical activity information, which are possibly important confounders.

In conclusion, our study found that increased VAT was independently associated with beta-cell dysfunction, and volumes of 5,059 cm<sup>3</sup> and above predicted prevalent impaired fasting glucose or T2DM in our participants who were moderately and severely obese. Given that measurements of VAT volume are not routinely performed in the clinical setting, SAD was found to provide a suitable proxy estimate which performed better than WC or BMI for identifying dysglycemia among high-adiposity women.

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## Abbreviations

<b>T2DM</b>	Type 2 diabetes mellitus
<b>VAT</b>	Visceral adipose tissue
<b>SAD</b>	Sagittal abdominal diameter
<b>WC</b>	Waist circumference
<b>BMI</b>	Body mass index
<b>Si</b>	Insulin sensitivity
<b>AIRg</b>	Acute insulin response to glucose
<b>DI</b>	Disposition index
<b>FSIGTT</b>	Frequently sampled intravenous glucose tolerance test
<b>FPG</b>	Fasting plasma glucose
<b>CT</b>	Computed tomography
<b>ROC</b>	Receiver operating curve

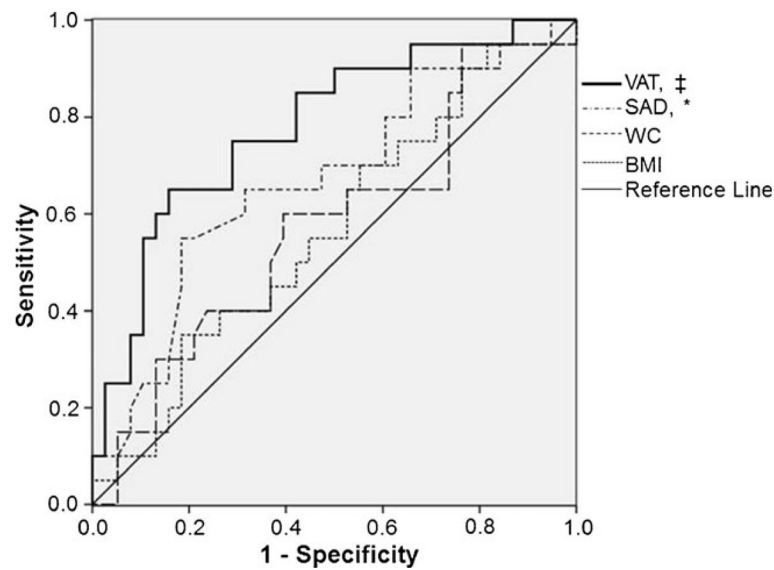
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**Fig. 1.**

Receiver operating characteristic curves of VAT, SAD, WC and BMI for prediction of dysglycemia in obese women. The reference line depicts a probability of 50 %, i.e., random chance. ‡ $P < 0.001$ , compared to the reference line; \* $P = 0.039$ , compared to the reference line. The optimal cut-points for each parameter (with their respective sensitivity and specificity) for distinguishing between normo- and dysglycemia appear are as follows: VAT, cut-off=5,059  $\text{cm}^3$ , sensitivity=65.0 %, specificity=85.0 %; SAD, cut-off 30.7 cm, sensitivity=55.0 %, specificity=80.0 %; WC, cut-off 132.7 cm, sensitivity= 60.0 %, specificity=60.5 %; BMI, cut-off=49.8  $\text{kg/m}^2$ , sensitivity= 35.0 %, specificity=80.0 %

**Table 1**

## Patient characteristics

	Normoglycemia	Dysglycemia
<i>n</i>	40	20
Age (years)	35.4±9.3	39.4±8.4
Body mass index (kg/m <sup>2</sup> )	46.0±5.2	47.0±5.9
Ancestry ( <i>n</i> , African American, Caucasian, Hispanic)	20;18;2	7;11;2
Visceral adipose tissue (cm <sup>3</sup> )	3,520±1550	5,440±1,840 <sup>‡</sup>
Subcutaneous abdominal adipose tissue (cm <sup>3</sup> )	13,780±2,770	15,400±5,310
Sagittal abdominal diameter (cm)	29.3±2.4	30.8±2.9 <sup>*</sup>
Waist circumference (cm)	128.5±14.9	131.9±14.4
Total adipose tissue (kg)	68.5±12.7	72.0±16.1
Glucose (mM)	4.60±0.46	6.94±1.62 <sup>‡</sup>
Insulin (mU/l)	12.25±6.45	15.78±11.44
HOMA-IR, (mU/lmM)	2.54±1.41	4.93±3.80 <sup>‡</sup>
HbA <sub>1c</sub> (%)	5.18±0.09	8.06±0.74 <sup>*</sup>
AIRg (μU ml <sup>-1</sup> min <sup>-1</sup> )	719±476	160±398 <sup>‡</sup>
Si (min <sup>-1</sup> μU <sup>-1</sup> ml <sup>-1</sup> )	1.91±1.10	1.55±0.97
DI (min <sup>-1</sup> )	1,220±800	180±460 <sup>‡</sup>

Moderately and severely obese women (*n*=60) were categorized as having fasting normoglycemia or dysglycemia (high fasting plasma glucose or frank type 2 diabetes). The demographic, adiposity, and metabolic indices are presented. The results are expressed as mean ± standard deviation of the mean

*HOMA-IR* homeostatic model assessment of insulin resistance, *AIRg* acute insulin response to glucose, *Si* insulin sensitivity, *DI* disposition index

Values depicted with symbols are significantly different from those in the normal glycemia group:

<sup>\*</sup> *P*<0.05;

<sup>‡</sup> *P*<0.005.

**Table 2**

Associations with AIRg and DI using general linear models

Independent variable	Beta coefficient ( $\pm$ SE)	P value
Model 1 — AIRg		
VAT volume	−0.363 (0.126)	0.006
Si	−0.352 (0.124)	0.007
Total adipose tissue	−0.361 (0.130)	0.007
Ancestry	−0.322 (0.137)	0.022
Age	−0.202 (0.153)	0.19
Menopausal status	−0.279 (0.152)	0.12
Model 2 — DI		
VAT volume	−0.363 (0.126)	0.005
Si	−0.375 (0.124)	0.004
Total adipose tissue	−0.412 (0.127)	0.002
Ancestry	−0.335 (0.130)	0.013
Age	−0.264 (0.148)	0.081
Menopausal status	−0.247 (0.161)	0.13

General linear modeling for the association of insulin secretion (*AIRg*) or the beta-cell function (*DI*) with visceral adipose tissue volume (*VAT*) when insulin sensitivity (*Si*), total adipose tissue, ancestry, age, and menopausal status were successively included as confounding variables in the model. Ancestry and menopausal status were categorical variables, the remaining were continuous. Standardized regression beta coefficient  $\pm$  SE, and *P* values are reported



**Table 3**

Associations of VAT with SAD and WC using linear modeling

	<b>Beta coefficient (<math>\pm</math>SE)</b>	<b>P value</b>
Model 1 — SAD		
SAD	0.42 (0.12)	0.001
Total adipose tissue	0.53 (0.16)	0.002
Age	0.44 (0.15)	0.006
Menopausal status	0.41 (0.17)	0.020
Ancestry	0.39 (0.17)	0.026
Model 2 — WC		
WC	0.27 (0.13)	0.039
Total adipose tissue	0.31 (0.19)	0.098
Age	0.20 (0.18)	0.25
Menopausal status	0.34 (0.18)	0.064
Ancestry	0.29 (0.19)	0.12

General linear modeling for the association of SAD or the WC with visceral adipose tissue volume (*VAT*) when total adipose tissue, age, menopausal status, and ancestry were successively included as confounding variables in the model. Ancestry and menopausal status were categorical variables, the remaining were continuous. Standardized regression beta coefficient  $\pm$  SE, and *P* values are reported